

Remarks

Support for the Amendments

The foregoing amendments to the specification are made to correct inadvertent typographical errors. Hence, these amendments do not introduce new matter, and their entry and consideration are respectfully requested.

Support for the amendments to claims 1, 13, 54, 58 and 59 can be found throughout the specification, specifically throughout pages 21-29. Hence, these amendments do not introduce new matter, and their entry and consideration are respectfully requested.

Status of the Claims

By the foregoing amendments, claims 1, 13, 54, 58 and 59 are sought to be amended. Upon entry of the foregoing amendments, claims 1, 3-6, 13-16, 34, 35, 54, 58 and 59 are pending in the application, with claims 1, 13 and 54 being the independent claims.

Summary of the Office Action

In the Office Action dated January 27, 2004, the Examiner has made seven rejections of the claims. Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

The Rejection Under 35 U.S.C. § 112, First Paragraph

In the Office Action at pages 3-5, section 6, the Examiner has rejected claims 1, 3-6, 13-16, 34, 35, 54, 58 and 59 under 35 U.S.C. § 112, first paragraph, as allegedly containing

subject matter which was not described in the specification in such a way as to reasonably convey to the ordinarily skilled artisan that the inventors, at the time the application was filed, had possession of the claimed invention. Applicants respectfully traverse this rejection.

The Examiner states ". . . Applicants did not define what a 'recombination site' is, therefore it can be interpreted as any nucleic acid sequence." Office Action at page 2, section 4. The Examiner further contends that Applicants only have possession of twenty-five species of nucleic acid molecules in a genus which comprises hundreds of millions of different possibilities. The Examiner also states that "at the time of filing, there is no record or description of which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise Ter-binding sites represented by SEQ ID NO:1-25." Office Action at page 5, second full paragraph. Applicants respectfully disagree with these statements and contentions.

Applicants respectfully submit that the phrase "recombination site" must be read as it would be interpreted by one of ordinary skill in the art. *See* M.P.E.P. § 2111.01. *See also* *Toro Co. v. White Consol. Indus., Inc.*, 199 F.3d 1295, 1299 ("[W]ords in patent claims are given their ordinary meaning in the usage of the field of the invention, unless the text of the patent makes clear that a words was used with a special meaning."). Applicants respectfully submit that the meaning of the term "recombination site" was well known in the art at the time of the filing of present Application (*see e.g.*, U.S. Patent Nos. 5,888,732, 6,143,557, 6,270,969 and 6,277,608). Applicants further submit that the ordinarily skilled artisan would readily understand that the term "recombination site" refers to specific nucleic acid sequences that allow for exchange of nucleic acid segments flanking these sequences

through the action of site-specific recombinases. *See id.* Non-limiting examples of recombination sites known to those skilled in the art include *att* sites and *lox* sites. *See id.* The Examiner's attention is directed to the present specification at page 49, paragraph [00146], where a non-limiting example of a recombination site, *attL*, is given. Applicants therefore respectfully submit that the ordinarily skilled artisan would readily understand the meaning of the term "recombination site," and accordingly would conclude, that at the time the application was filed, Applicants had full possession of the claimed invention.

Present claim 1 (and hence, claims 3-6, 34, 35, 58 and 59 that depend ultimately therefrom and that are also rejected) recites an isolated nucleic acid molecule comprising at least one Ter-site and further comprising at least one recombination site. Similarly, present claim 13 (and hence, claims 14-16 that depend ultimately therefrom and that are also rejected) recites a solid support comprising at least one oligonucleotide comprising at least one Ter-site and further comprising at least one recombination site.

Applicants respectfully submit that the present specification provides adequate written description for the presently claimed nucleic acid molecules, and solid supports comprising oligonucleotides, which comprise at least one Ter-site and at least one recombination site. Applicants wish to remind the Examiner that "[a]dequate description under the first paragraph of 35 U.S.C. 112 does not require literal support for the claimed invention . . . the observation of a lack of literal support does not, in and of itself, establish a *prima facie* case for lack of adequate descriptive support under the first paragraph of 35 U.S.C. 112." *Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. Int. 1994). Instead, the written description requirement of 35 U.S.C. § 112, first paragraph, is met "if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that

an [applicant] had possession of the concept of what is claimed," *id.*, *i.e.*, "[i]f a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification" *In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996). An applicant is not required to disclose or provide a working example of every species of a given genus in order to meet the written description requirement of 35 U.S.C. § 112 (*see Parks and Alton*), and subject matter that "might fairly be deduced from the original application" is considered to be described in the application as filed. *Acme Highway Products Corp. v. D.S. Brown Co.*, 431 F.2d 1074, 1080 (6th Cir. 1970) (citations omitted), *cert. denied*, 401 U.S. 956 (1971), *followed by Westphal v. Fawzi*, 666 F.2d 575, 577 (C.C.P.A. 1981). Moreover:

[a] description of a genus of [nucleic acid molecules] may be achieved by means of a recitation of a representative number of [nucleic acid molecules], defined by nucleotide sequence, falling within the scope of the genus

Regents of Univ. of Calif. v. Eli Lilly & Co., 119 F.3d 1559, 1569 (Fed. Cir. 1997).

The present specification describes a number of representative examples of the claimed genus of Ter-sites (*see* present specification at pages 22-23). As noted above, the ordinarily skilled artisan would readily understand what is meant by the term "recombination site" and also could readily identify a number of representative examples of recombination sites for use in the practice of the presently claimed invention. Hence, the "representative number" standard under *Eli Lilly*, upon which the Written Description Guidelines (M.P.E.P. § 2163) are based, is clearly met by the present specification. Applicants respectfully assert that the present specification provides sufficient written description to convey to one of

ordinary skill that Applicants had possession of the full scope of the claimed invention upon filing of the Application.

In view of the foregoing remarks, Applicants respectfully submit that the ordinarily skilled artisan would readily recognize that Applicants were in full possession of the claimed invention at the time the Application was filed. Applicants respectfully request that the rejection of claims 1, 3-6, 13-16, 34, 35, 54, 58 and 59 under 35 U.S.C. § 112, first paragraph, be reconsidered and withdrawn.

The Rejections Under 35 U.S.C. § 112, Second Paragraph

In the Office Action at page 5, section 7, the Examiner has rejected claims 16 and 58 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse these rejections.

The Examiner has first rejected claim 16 under 35 U.S.C. § 112, second paragraph, stating that there is insufficient antecedent basis for the term "Ter-site" in claims 13 and 15 from which claim 16 depends. Applicants respectfully disagree. However, solely to expedite prosecution, and not in acquiescence to this rejection, claim 13 has been amended to recite "Ter-site." Applicants respectfully submit that there is sufficient antecedent basis for the term "Ter-site" in claims 13 and 15. In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 16 under 35 U.S.C. § 112, second paragraph.

The Examiner has next rejected claim 58 under 35 U.S.C. § 112, second paragraph, asserting that there is insufficient antecedent basis for the term "Ter sites" in claim 1 from

which claim 58 depends. The Examiner further contends that claim 58 is indefinite over the recitation "wherein the at least Ter-sites." Applicants respectfully disagree. However, solely to expedite prosecution, and not in acquiescence to this rejection, claim 58 has been amended to recite "the at least two Ter-sites." Applicants respectfully submit that there is sufficient antecedent basis for this phrase in claim 1 and that this phrase is not indefinite. In view of the foregoing remarks, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 58 under 35 U.S.C. § 112, second paragraph.

The Rejection Under 35 U.S.C. § 102(b) Over Lee

In the Office Action at pages 6-7, section 9, the Examiner has rejected claims 1, 3-6, 34, 58 and 59 under 35 U.S.C. § 102(b), as being allegedly anticipated by Lee *et al.* (*J. Biol. Chem.* 267:8778-8784 (1992); hereinafter "Lee") and evidenced by Bussiere *et al.* (*Mol. Microbiol.* 31:1611-1618 (1999); hereinafter "Bussiere"). Applicants respectfully traverse this rejection.

The Examiner contends that Lee discloses an isolated nucleic acid molecule engineered to comprise two Ter-sites (including TerB) and an origin of replication. The Examiner further contends that the Ter-sites are arranged in such a way that the sequence between the Ter-sites which does not contain the origin of replication is not replicated in cells expressing a replication termination protein. The Examiner further contends that Lee discloses plasmids and compositions comprising Ter-binding proteins. The Examiner relies on the disclosure of Bussiere to confirm that the Ter-binding protein from *E. coli* is the same as the Tus protein. The Examiner therefore concludes that Lee discloses the presently claimed invention. Applicants respectfully disagree with this conclusion.

As noted above, present claim 1 (and hence, claims 3-6, 34, 58 and 59 that depend ultimately therefrom and that are also rejected over Lee) recites an isolated nucleic acid molecule comprising at least one Ter-site and further comprising at least one recombination site.

Applicants respectfully submit that Lee does not disclose every element of claim 1 (and hence the dependent claims noted above), and therefore cannot anticipate the claimed invention. Under 35 U.S.C. § 102, a claim can only be anticipated if every element in the claim is expressly or inherently disclosed in a single prior art reference. *See Kalman v. Kimberly Clark Corp.*, 713 F.2d 760, 771 (Fed. Cir. 1983), *cert. denied*, 465 U.S. 1026 (1984).

As discussed in the previous reply, dated November 4, 2003 (incorporated by reference herein in its entirety), Applicants submit that Lee does not disclose an isolated nucleic acid molecule comprising at least one Ter-site and further comprising at least one recombination site. As discussed above, the ordinarily skilled artisan would readily understand what is meant by the term "recombination site" and could also readily identify a representative number of recombination sites that could be used in the practice of the present invention, e.g., *att*, *lox*, etc. Lee does not disclose recombination sites as that term is used in the present specification and claims, much less an isolated nucleic acid molecule comprising a Ter-site and a recombination site. Applicants respectfully submit that Lee therefore does not disclose every element of the present claims.

Hence, in view of *Kalman*, Lee cannot and does not anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection of claims 1, 3-6, 34, 58 and 59 under 35 U.S.C. § 102(b) over Lee are respectfully requested.

The Rejection Under 35 U.S.C. § 102(a) Over Neylon

In the Office Action at page 7, section 10, the Examiner has rejected claims 13 and 14 under 35 U.S.C. § 102(a), as being allegedly anticipated by Neylon *et al.* (*Biochemistry* 39:11989-11999 (2000); hereinafter "Neylon") and evidenced by Jönsson *et al.* (*Biotechniques* 11:620-627 (1991); hereinafter "Jönsson"). Applicants respectfully traverse this rejection.

As noted above, present claim 13 (and hence, claim 14 which depends ultimately therefore and that is also rejected over Neylon) recites a solid support comprising at least one oligonucleotide comprising at least one Ter-site and further comprising at least one recombination site. As discussed in the previous reply, dated November 4, 2003, Applicants submit that Neylon does not disclose such a solid support.

Neylon does not disclose recombination sites as that term is used in the present specification and claims, much less a solid support comprising at least one oligonucleotide comprising at least one Ter-site and further comprising at least one recombination site. Hence, Neylon does not disclose every element of the present claims.

Therefore, in view of *Kalman*, Neylon cannot and does not anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection of claims 13 and 14 under 35 U.S.C. § 102(a) over Neylon are respectfully requested.

The Rejection Under 35 U.S.C. § 102(b) Over Pace

In the Office Action at page 7, section 11, the Examiner has rejected claim 54 under 35 U.S.C. § 102(a), as being allegedly anticipated by Pace *et al.* (U.S. Patent No. 5,681,736; hereinafter “Pace”). Applicants respectfully traverse this rejection.

Present claims 54 recites a kit comprising an isolated nucleic acid molecule comprising at least one Ter-site and further comprising at least one recombination site, the kit further comprising one or more components selected from a group consisting of one or more Ter-binding proteins, one or more nucleotides, one or more DNA polymerases, one or more reverse transcriptases, one or more suitable buffers, one or more primers, one or more recombination proteins, instructions, and one or more terminating agents.

Applicants respectfully submit that Pace does not disclose a kit comprising an isolated nucleic acid molecule comprising at least one Ter- site and further comprising at least one recombination site as that term is used in the present specification and claims. Hence, Pace does not disclose every element of the presently claims.

Therefore, in view of *Kalman*, Pace cannot and does not anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection of claim 54 under 35 U.S.C. § 102(b) over Pace are respectfully requested.

The Rejection Under 35 U.S.C. § 103(a) Over Neylon in view of Gold

In the Office Action at page 8, section 13, the Examiner has rejected claims 15 and 16 under 35 U.S.C. § 103(a), as being allegedly anticipated by Neylon in view of Gold *et al.* (U.S. Patent No. 6,242,246; hereinafter “Gold”). Applicants respectfully traverse this rejection.

The Examiner contends that Neylon discloses an assay which includes binding of TUs to double stranded Ter-sites, but that Neylon does not disclose oligonucleotides capable of forming a stem-loop or hairpin, or oligonucleotides with Ter-sites in the duplex portion of the stem-loop or hairpin. The Examiner relies on Gold to cure this deficiency, and concludes that it would have been *prima facie* obvious to have used the hairpin nucleic acids of Gold in the assays of Neylon to construct the solid supports of the present claims. Applicants respectfully disagree with these conclusions.

As noted above, present claim 13, from which claims 15 and 16 ultimately depend, recites a solid support comprising at least one oligonucleotide comprising at least one Ter-site and further comprising at least one recombination site. As noted above, Neylon does not disclose such a solid support, and hence cannot support a *prima facie* case of obviousness. This serious deficiency in Neylon is not cured by the disclosure of Gold, as Gold does not disclose recombination sites as that term is used in the present specification and claims, much less a solid support comprising at least one oligonucleotide comprising at least one Ter-site and further comprising at least one recombination site. Therefore, Neylon and Gold, alone or in combination, do not disclose or suggest the presently claimed invention.

In view of the foregoing remarks, Applicants respectfully submit that Neylon, in view of Gold, cannot support a *prima facie* case of obviousness. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claims 15 and 16 under 35 U.S.C. § 103(a).

Conclusion

All of the stated grounds of rejection have been properly traversed or otherwise overcome. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn.

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

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